# Editorial

## RECENT STUDIES ON SILICOSIS

SILICON, in its many combinations and derivatives, is one of the most widely distributed elements in nature. It is found in many rocks and minerals, in most foodstuffs, particularly those of vegetable origin, and in nearly all dust. Consequently, it is constantly entering the animal body, and, to some extent, therefore, may be regarded as a normal constituent thereof. It has definitely been shown that silica in solution can exert a toxic action on the tissues. For example, it can produce coagulation necrosis of cells, fatty degeneration of the heart muscle, and necrosis of the liver parenchyma. That it does not produce harmful effects more often is perhaps linked up with the fact that it is readily excreted, the renal threshold for silica being low, as King, Stantial and Dolan[1] have proved. The dosage, also, would naturally have to be taken into account here. At any rate, so far as our present information goes, there is only one situation in the human body where the presence of silica is associated with pathological change, namely, the lung. The peculiar, and apparently specific, lesions in this organ attributed to silica are due to the inhalation of dust over prolonged periods, and are particularly related to certain occupations, such as mining, stone-cutting, sand-blasting, tool, axe, glass, slate, porcelain and silica grinding, moulding, vitreous enamel spraying, and abrasive soap manufacturing. Rarely, silicosis may develop where we would not suspect it, as in cotton-carders and in those engaged in polishing the heels of boots.

The chronic lesions produced in the lung by the inhalation of dust have been grouped in the past under the term "pneumonokoniosis," and a variety of this, due to silicon, was known as "silicosis." The Committee on Pneumonokoniosis of the Industrial Section of the American Public Health Association recently defined silicosis as

> "a disease due to breathing air containing silica ($SiO_2$), characterized anatomically by generalized fibrotic changes and the development of miliary nodulation in both lungs, and clinically by shortness of breath, decreased chest expansion, lessened capacity for work, absence of fever, increased susceptibility to tuberculosis (some or all of which symptoms may be present), and by characteristic x-ray findings."

This definition, which, as a matter of fact, is a description rather than a definition, by intention excludes disease produced by other kinds of dust, such as coal, asbestos, and talc dust. It is questionable if this is justifiable. For purposes of workmen's compensation silicosis is defined in Ontario more briefly as "fibrosis of the lungs due to the inhalation of silica dust."

The pathogenesis of silicosis may be epitomized as follows. The affection begins as a dry bronchiolitis. Dust-laden phagocytes accumulate in and about the intrapulmonary lymphoid tissue and pass into the lymphatics of the lung, eventually reaching the tracheo-bronchial lymph-nodes. Fibrous tissue gradually develops within these aggregations of phagocytes and characteristic laminated, hyaline, fibrous nodules are produced which ultimately undergo degeneration. These nodules gradually enlarge by extension at their periphery, so that further areas of pulmonary tissue become involved. It may prove to be the case, however, that the first manifestations of silicosis occur in the tracheo-bronchial lymph-nodes. The sequence of events is important.

Silicosis presents certain peculiar features, is a deadly disease, and constitutes in many countries a serious industrial hazard, so that it is not surprising that it has attracted widespread attention in recent years. Much good work has been done in Great Britain, South Africa, Canada, and the United States, partly in elucidating its pathogenesis and pathology, and partly in devising preventive

1. KING, E. J. AND STANTIAL, H.: Biochemistry of silicic acid, *Biochem. J.*, 1933, **27**: 990.
KING, E. J., STANTIAL, H. AND DOLAN, M.: Biochemistry of silicic acid, *ibid.*, 1933, **27**: 1002, 1007.

measures. In this connection we might cite certain papers emanating from the Banting Institute, Toronto, the most recent of which have been appearing in our *Journal*.[2] But despite intensive study many important points remain unsettled. We may ask, here, several questions. Is silicosis merely one form of pneumonokoniosis, or is all pneumonokoniosis silicosis? Is the agent which produces such serious changes in the lung silica, some other derivative of silicon, or a combination of substances, some siliceous and some not? What is the relationship between pulmonary tuberculosis and silicosis? What is the most efficient method of prevention?

From the pathologist's point of view it can be at once stated that there is room for the generic term "pneumonokoniosis", to cover all cases in which there is inhalation of dust with attendant tissue changes. We note that Prof. M. J. Stewart, of Leeds, adheres to the classical division of pneumonokoniosis into anthracosis, silicosis, and siderosis, and adds the recently described entity, asbestosis. As asbestos is a silicate there seems to be no very good reason for separating it from other forms of silicosis, unless, indeed, on the basis of a somewhat different morbid anatomy. But, it has to be admitted that many dusts are comparatively innocuous, and, from the clinical point of view, silicosis is the all-important form of pneumonokoniosis. Naturally, many dusts are compounds of varying substances. Thus, coal-miners, notably those working with anthracite, are exposed to mixtures of carbon and silica, and hæmatite workers, as in west Cumberland, England, to iron and silica. Usually it is to the silicotic element ($SiO_2$) to which the harmful effects in silicosis are attributed. More experimentation will be required before the relative degrees of toxicity of the various components of dust can be determined. This point has a bearing on the question of the relationship of silicosis and tuberculosis. Some recent work of Prof. E. H. Kettle[3] gives promise of affording us a ready means of classifying dusts. We quote the *Lancet's* account of this study (*The Lancet*, 1934, **1**: 904). "Where a noxious dust reaches the lung through inhalation or through intratracheal injection, the first lesion to be observed is in the glands at its base. As early as three months after intratracheal injection of a suspension of crystalline silica, or of finely ground flint, changes can be observed in the pulmonary glands long before true silicotic lesions in the lungs are visible; but that these ultimately develop was shown by the examination of other animals in the same series which were allowed to survive for much longer periods. Control experiments with iron-coated silica and wellingtonite, both being inert dusts, showed merely a copious deposition of dust without any cellular activity or fibrosis. Since these observations were only incidental to the main object of the experiments, which was the study of the later pulmonary lesions, the earliest date at which the changes can be found was not ascertained. But it is clear that in the short space of three months or less it should be possible to estimate whether any given dust is likely to be among the active or inert dusts, though it is not claimed that a dust can be finally incriminated on indirect observations. Application of the method on a large scale might well result not only in a definite preliminary classification of dusts but in the establishment of standards by which any samples could be tested."

Until recently it has been fairly widely accepted that silicosis is due to the accumulation of silica (silicon dioxide, $SiO_2$) in the lungs. This silica does not produce its effects by mechanical irritation leading to death of phagocytes and productive fibrosis; rather, it is the silica which goes into solution that is toxic. Solution occurs through the action of alkaline substances and $CO_2$, both of which, of course, can be found in the lymph and blood plasma of the lung, as elsewhere. This explanation is now doubted by some. W. R. Jones[4] believes that a compound silicate—sericite—is the true cause of

2. KING, E. J. AND DOLAN, M.: Silicosis and the metabolism of silica, *Canad. M. Ass. J.*, 1934, **31**: 21.
IRWIN, D. A.: The histological demonstration of siliceous material by microincineration, *ibid.*, 1934, **31**: 135.
IRWIN, D. A.: Microincineration as an aid in the diagnosis of silicosis, *ibid.*, 1934, **31**: 140.
ROBSON, W. D., IRWIN, D. A. AND KING, E. J.: Experimental silicosis, quartz, sericite, and irritating gases, *ibid.*, 1934, **31**: 237.
FRANKS, W. R.: Silica dust, *ibid.*, 1934, **31**: 245.

3. KETTLE, E. H.: The detection of dangerous dusts, *The Lancet*, 1934, **1**: 889.

4. JONES, W. R.: Silicotic lungs; minerals they contain, *J. of Hygiene*, 1933, **33**: 307.

silicosis. In this he is supported by Lyle Cummins, of Cardiff. Sericite belongs to the mica group and is a modification of muscovite, which is a hydrated potassium-aluminium silicate, but with varying amounts of $SiO_2$ in the molecule. It is somewhat fibrous, like asbestos, which can also produce fibrotic changes in the lungs. Jones' view is supported by the peculiar fact that silicosis is very frequent in the gold-miners of the Transvaal and rare in the Kolar gold-miners of India though much quartz dust is produced in the workings in both places. Similar differences in the distribution and frequency of silicosis have been noted also in Scotland, Wales and elsewhere. Prof. Lyle Cummins[5] and Dr. Sladden think that Dr. Jones has made out a very good case in regard to the etiology of silicosis, and that his views, if confirmed, will explain many points now obscure in connection with the etiology of the disease. The point is being enquired into in various places at the present time, but cannot be considered as settled. The Canadian workers, Robson, Irwin, and King,[6] do not find that sericite plays the leading rôle. These last mentioned observers have also (*loc. cit.*) investigated the part played by irritating gases, such as are produced in blasting, in the production of silicosis. They have found that when $NO_2$ and $SO_2$ are inhaled by the experimental animals degenerative lesions in the lungs and pneumonitis resulted. When these gases were inhaled together with silica dust a rapidly developing (acute) silicosis was produced.

It has long been known that silicosis and pulmonary tuberculosis were apt to be associated, to a degree that could not be attributed to coincidence. A large proportion of silicotic miners die of tuberculosis. On the other hand, coal miners, even if silicotic, tend to escape tuberculosis. Various theories have been advanced to explain this. One is that mechanical injury, by destroying many of the phagocytes in the lung lessens the resistance of the pulmonary tissues and so favours the spread of infection. This can hardly be substantiated, for the theory would apply equally well to cases of anthracosis, in which, as we have stated, tuberculosis is not a common concomitant. Another theory is that silica in solution exerts a toxic and depressing influence on the cells, and, moreover, actually promotes the growth and activity of the tubercle bacillus. Prof. E. H. Kettle, in particular has investigated this question.[7] He introduced into experimental animals, intratracheally, suspensions of various kinds of dust, with and without the addition of tubercle bacilli. Using an emulsion of killed tubercle bacilli, so as to mitigate the reaction, he found that when he introduced these with the active dusts the fibrotic process was accelerated, while the inert dusts remained quiescent in the pulmonary tissues or were gradually phagocytosed. He has found analogous results when the materials employed were injected subcutaneously. Experiments have also been made by other observers to determine the effect of adding silica to culture media on the growth of the tubercle bacillus. Some report an acceleration of growth under these conditions, but at the moment the findings require further confirmation and are not convincing.

In determining the relative rôles played by silica and the tubercle bacillus, it would seem desirable to determine, if possible, which condition comes first, tuberculosis or silicosis. This may be important. Bellander[8] has advanced the idea that if tuberculosis has been in existence first a certain degree of silicosis may be, perhaps, of as much therapeutic value as a pneumothorax. Yet, though silicosis, by hastening cicatrization about a tuberculous focus, may delay the spread of the tuberculosis, the action of tuberculosis on previously existing silicosis is quite another matter. Attempts should be made to see if there is anything in this.

A.G.N.

5. CUMMINS, L. AND SLADDEN, A. F.: Letter in *Brit. M. J.*, 1934, **1**: 554.
6. ROBSON, W. D., IRWIN, D. A. AND KING, E. J.: Experimental silicosis; quartz, sericite, and irritating gases, *Canad. M. Ass. J.*, 1934, **31**:
7. KETTLE, E. H.: Experimental pneumoconiosis; infective silicatosis, *J. Path. & Bact.*, 1934, **38**: 201.
8. BELLANDER, J.: Silicosis in workers engaged in metal polishing and relation to tuberculosis, *Hygiea*, 1933, **95**: 655.